Methylpyridylbenzimidazoles. Part I. Mono, bis-Quaternary Salts and Related Polymethyne Dyes

Ermanno Barni, Piero Savarino and Guido Viscardi

Istituto di Chimica Organica Industriale, Università di Torino, Corso Massimo D'Azeglio 48, 10125 Torino, Italy

Ezio Pelizzetti

Istituto di Chimica Analitica, Università di Torino, via Pietro Giuria 5, 10125 Torino, Italy

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The reaction of 2-(4-methyl-2-pyridyl)benzimidazole with long chain alkyl halides led to *N*-alkylation at the imidazole ring. The bases obtained were selectively quaternized at the azine and azole nitrogen atoms. The pyridinium salts gave the corresponding polymethyne dyes. Spectral (nmr and uv) and surface properties are briefly discussed.

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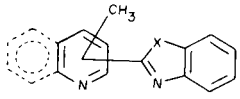
Our studies on the synthesis and properties of 2-(methylpyridyl or quinolyl)benz-X-azoles led us recently to consider the effect of the relative position of the rings in system



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1 on the site of quaternisation (1-4). In particular, for 2-(4-methyl-2-pyridyl)benzimidazole (**1**) (1) we were able to isolate a *N,N*-dimethylbenzimidazolium salt by reaction with methyl iodide (4), from which a polymethine dye could not be prepared. On the other hand, by reaction of **1** with dimethylsulphate in toluene, it was possible to isolate a doubly charged salt from which a cyanine dye was prepared (5).

This paper deals with salts and dyes derived from new bases (2-4) prepared by the reaction of **1** with long alkyl chain bromides as indicated in the following scheme:

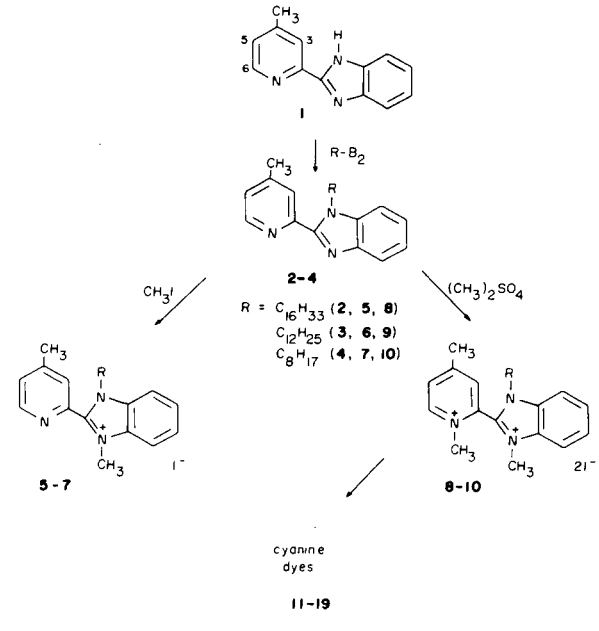


Table I

Characterisation Data on Methylpyridylbenzimidazoles and Related Salts

Compound number	Yield %	Mp °C	R_f	Empirical formula	Elemental analyses C% Calcd.	C% Found	H% Calcd.	H% Found	N% Calcd.	N% Found	log CMC	Amin(a) (Å²)
2	50	51-53	0.86	$C_{29}H_{43}N_3$	80.32	80.39	9.99	10.04	9.69	9.80	—	—
3	47	32-34	0.84	$C_{25}H_{35}N_3$	79.53	79.47	9.34	9.42	11.13	11.05	—	—
4	43	17-19	0.82	$C_{21}H_{27}N_3$	78.46	78.64	8.47	8.35	13.07	13.11	—	—
5	24	133-134	0.15	$C_{30}H_{46}IN_3$	62.60	62.80	8.06	8.13	7.30	7.28	—	82
6	23	135-136	0.14	$C_{26}H_{38}IN_3$	60.11	60.11	7.37	7.49	8.09	8.16	—	68
7	22	128-129	0.10	$C_{22}H_{30}IN_3$	57.02	56.90	6.53	6.61	9.07	9.07	—	80
8	71	141-143	0.35	$C_{31}H_{49}I_2N_3$	51.89	51.74	6.88	6.93	5.86	5.97	-3.03	115
9	65	131-132	0.34	$C_{27}H_{41}I_2N_3$	49.03	49.18	6.25	6.12	6.35	6.40	-2.30	109
10	76	123-124	0.33	$C_{23}H_{33}I_2N_3$	45.63	45.60	5.49	5.58	6.94	7.07	-1.34	118

(a) Minimum areas per molecule.

Table II

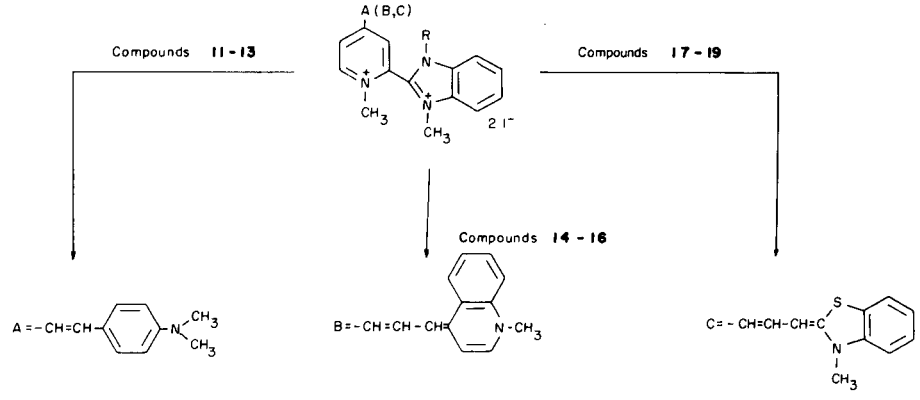
Spectroscopic Data on Methylpyridylbenzimidazoles and Related Salts

Compound number	Electronic absorption spectra (a) λ max (nm)	log ε	NMR Spectra τ (ppm) $\geq C-CH_3$	$\geq N-CH_2-$ (b)	$\geq \overset{+}{N}-CH_3$ (azine)	$\geq \overset{+}{N}-CH_3$ (azole)	H_3	H_5	H_6	(d) Benzimidazole protons
1	308	4.40	7.55	—	—	—	1.77	2.67 (c)	1.43	—
2	302	4.28	7.53	5.17	—	—	1.83	2.67 (c)	1.43	3.03-2.27
3	302	4.28	7.53	5.17	—	—	1.83	2.67 (c)	1.43	3.03-2.27
4	302	4.28	7.53	5.17	—	—	1.83	2.67 (c)	1.43	3.03-2.27
5	282	4.19	7.45	5.45	—	5.95	1.88	2.27 (c)	1.17	2.36-1.67
6	282	4.19	7.43	5.45	—	5.95	1.88	2.27 (c)	1.17	2.33-1.67
7	282	4.19	7.46	5.45	—	5.95	1.88	2.27 (c)	1.17	2.36-1.63
8	284	4.04	7.23	5.46	5.80	5.97	1.28	1.52	0.52	2.23-1.63
9	284	4.04	7.25	5.46	5.80	5.97	1.30	1.52	0.53	2.23-1.63
10	284	4.04	7.23	5.46	5.80	5.97	1.28	1.50	0.52	2.23-1.63

(a) The main absorptions above 250 nm are indicated. (b) First methylene protons of the long chain linked to the azole nitrogen. In compounds **5-10**, the azole nitrogen could be charged by resonance effects. (c) Partially superimposed to the signals of the benzimidazole protons. (d) The resonance range for the multiplet is indicated.

Table III

Polymethine Dyes



Compound number	R =	Yield %	Mp °C	R_f	Empirical formula	Elemental Analyses C% Calcd.	C% Found	H% Calcd.	H% Found	N% Calcd.	N% Found	Electronic absorption spectra °C λ max (nm)	log ε	log CMC	A min (a)(Å²)
11	$C_{16}H_{33}$	80	152-154	0.13	$C_{40}H_{58}I_2N_4$	56.61	56.80	6.89	6.97	6.60	6.65	558	4.58	-3.68	96
12	$C_{12}H_{25}$	66	150-152	0.12	$C_{36}H_{50}I_2N_4$	54.55	54.61	6.36	6.48	7.07	7.10	558	4.58	-3.21	96
13	C_8H_{17}	40	148-150	0.12	$C_{32}H_{42}I_2N_4$	52.18	52.20	5.75	5.87	7.61	7.50	558	4.58	-2.26	109
14	$C_{16}H_{33}$	49	158-160	0.13	$C_{43}H_{58}I_2N_4$	58.37	58.29	6.61	6.59	6.33	6.40	676	5.09	-3.80	133
15	$C_{12}H_{25}$	46	155-157	0.12	$C_{39}H_{50}I_2N_4$	56.53	56.48	6.08	6.13	6.76	6.66	676	5.09	-2.79	151
16	C_8H_{17}	41	150-152	0.10	$C_{35}H_{42}I_2N_4$	54.41	54.52	5.48	5.56	7.25	7.30	676	5.09	-2.10	162
17	$C_{16}H_{33}$	23	158-160	0.13	$C_{41}H_{56}I_2N_4S$	55.28	55.17	6.34	6.40	6.29	6.19	605	5.03	-3.55	174
18	$C_{12}H_{25}$	27	162-164	0.12	$C_{37}H_{48}I_2N_4S$	53.24	53.37	5.80	5.92	6.71	6.81	605	5.03	-2.84	216
19	C_8H_{17}	29	167-169	0.11	$C_{33}H_{40}I_2N_4S$	50.91	50.77	5.18	5.25	7.20	7.06	605	5.03	-1.80	240

(a) Minimum areas per molecule.

The formation of alkyl derivatives was controlled by the relative amount of the reagents. A 50% yield is highly satisfactory because one mole of **1** acts as a base in capturing hydrogen bromide formed in the reaction.

The bases **2-4**, upon reacting with methyl iodide, gave the benzimidazolium salts **5-7** from which cyanine dyes were not obtained. On the other hand, by reaction of **2-4** with dimethylsulphate, followed by an exchange with potassium iodide, the salts **8-10** were recovered. This behaviour is similar to that previously observed for compound **1** (4,5).

Physical constants, analyses and spectroscopic data for componds **2-10** are reported in Tables I and II.

The presence of long alkyl chains in the benzimidazole moiety of **1** markedly lowers the melting point in proportion to the length of the chain. This situation is probably due to loss of intermolecular hydrogen bonding. These enhanced hydrophobic properties are also responsible for the high R_f values on Silica gel (eluent BAW). All of the R_f values are in the range 0.86-0.82, while the R_f of **1** is 0.41.

The electronic spectra of compounds **2-4** are, as expected, identical in spite of the different chain lengths. The absorption maxima show weak hypso and hypochromic effects compared to compound **1**. The nmr spectra of compound **1** and of its long chain counterparts **2-4** are practically the same, except for the presence of signals from aliphatic protons. The analysis of chemical shift values agrees with the assigned structures. If, by reaction of R-X with **1**, quaternisation at azine or azole *N*-atoms instead of *N*-alkylation were to take place, a downfield shift for the same aromatic and methyl protons would be observed.

The benzimidazolium salts **5-7**, if compared with the starting long chain bases, have distinctly higher melting points, lower R_f values, a strong hypsochromic and a moderate hypochromic effect. Again, the proton resonance positions agree with the assigned structures of monomethiodides at the imidazole nitrogen atoms. In fact, due to this charge location, signals from the pyridine methyl and aromatic protons are only weakly shifted downfield whereas a considerably stronger effect is apparent for the benzimidazole protons.

A further investigation of nmr and electronic spectra gives information on a reasonable distortion of the planes of the pyridine and benzimidazole moieties. The $^{+}N\text{-}CH_2$— (triplet) signals from the salts are shifted upfield to a surprising extent with respect to those from the corresponding bases, probably indicating an anisotropic effect due to the non-coplanarity of the rings. Such deductions are further supports if hypso and hypochromic effects in the elecronic spectra are taken into consideration. The distortion is also shown in *N*-alkylated bases in comparison to **1** as evinced by the above mentioned feeble hypso and hypochromic effects and by further chemical evidence: these heterocycles contain a ferroin type system which should be able to complex transition metal ions; in fact, while compound **1** gave a complex with ferrous ions (6), the long chain counterparts did not react.

The bisquaternary salts **8-10**, if compared to the monoquaternary ones, have melting points of the same order of magnitude, surprisingly higher R_f values, a very weak bathochromic and an appreciable hypochromic shift. This is a reasonable consequence of the introduction of a further positive charge and a methyl group into the previously distorted chromogen (Figure 1).

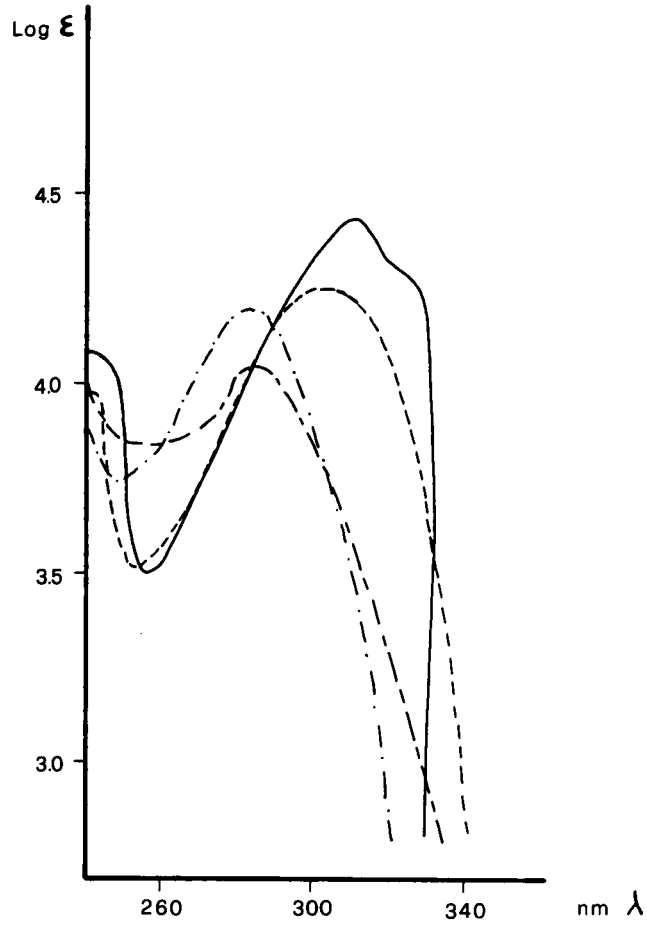


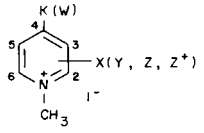
Figure 1. Electronic absorption spectra.

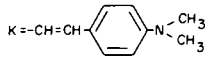
The nmr data confirm the doubly charged structure. In fact, in comparison with monomethiodides, the signals of benzimidazole protons practically have the same position, whereas pyridine methyl and aromatic protons display their resonances considerably downfield.

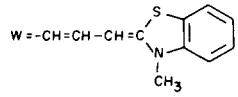
From the salts **8-10** a series of polymethine dyes were prepared and their analytical and spectroscopic data are reported in Table III. Some comments can be made on the colour-constitution relationships in these dyes. The absorption maxima in alcoholic solution obey Beer's law and are not influenced by the aliphatic chain length; as expected, a bathochromic effect of unsymmetrical *vs* styryl and lepidine **14-16** *vs* benzothiazole **17-19** dyes was observed; data in Table IV show the bathochromic effect of benz-X-azolyls (stronger in styryl than in unsymmetrical dyes) previously mentioned (**2-4**), which reaches a max-

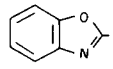
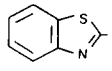
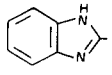
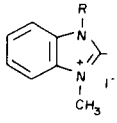
Table IV

Effect of Benz-X-azolyls on the Absorption of Dyes







Structure		λ max (nm)	log ε	λ max (nm)	log ε
X = 	H (a)	480	4.62	557	4.98
	3-X (a)	535	4.63	596	4.95
Y = 	2-X (b)	531	4.59	601	4.92
Z = 	3-Y (a)	524	4.60	590	4.89
Z+ = 	3-Z (c)	515	4.57	564	4.84
	2-Z+	558	4.58	605	5.03

(a) Taken from ref (3). (b) Taken from ref (2). (c) Taken from ref (4).

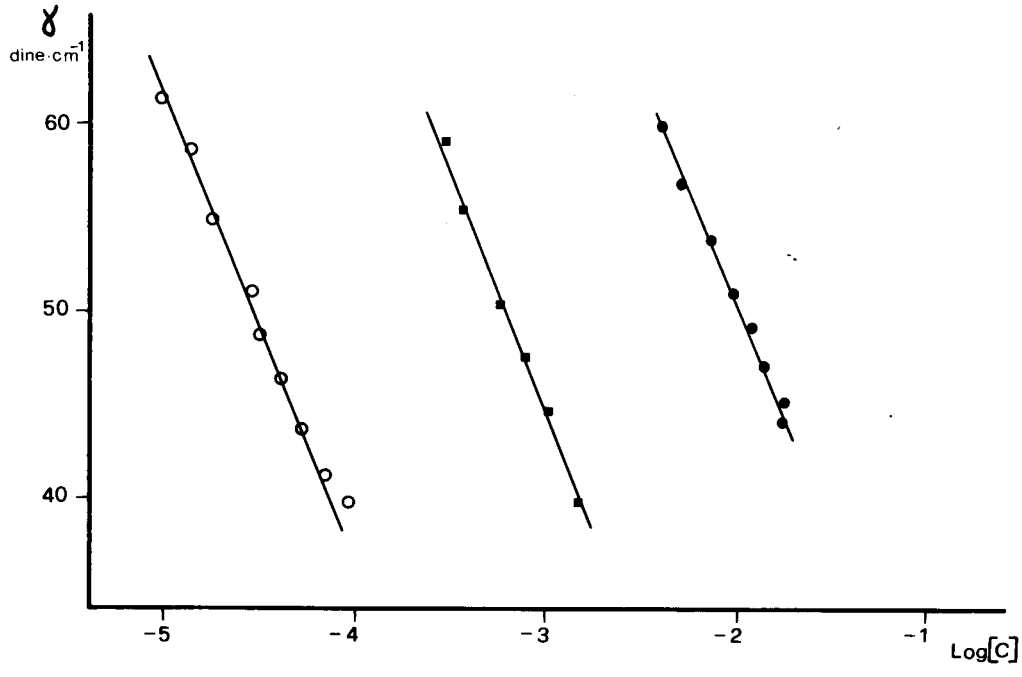


Figure 2. O Compound **5** (R = $C_{16}H_{33}$)
■ Compound **6** (R = $C_{12}H_{25}$)
● Compound **7** (R = C_8H_{17})

Figure 2. Surface tension (γ) as a function of the logarithm of the molar concentration of mono-charged benzimidazolium salts.

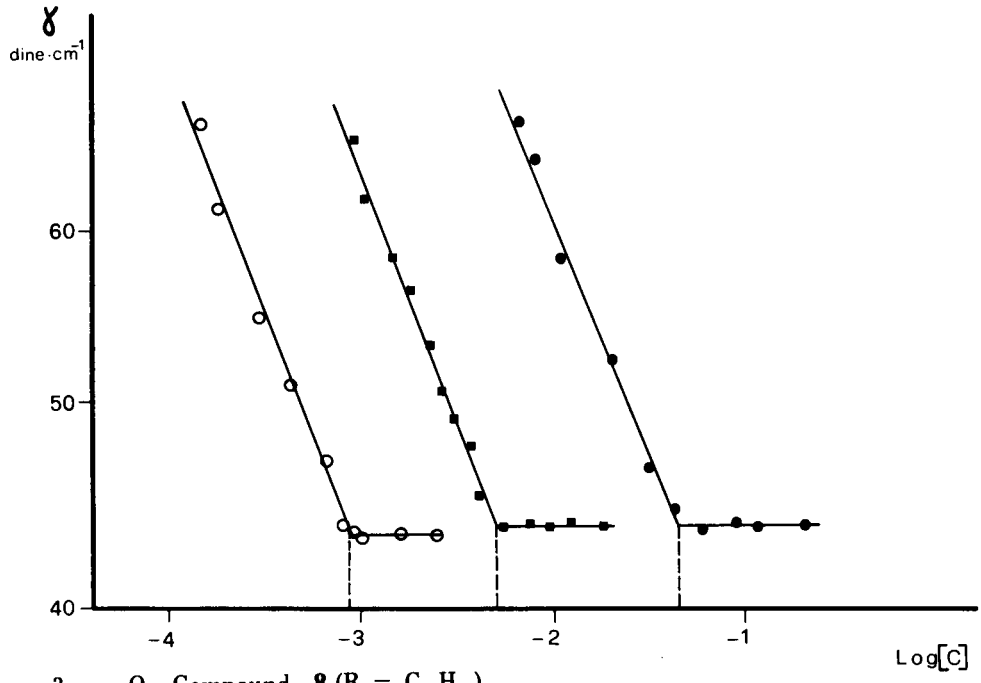


Figure 3. ○ Compound **8** (R = $C_{16}H_{33}$)
■ Compound **9** (R = $C_{12}H_{25}$)
● Compound **10** (R = C_8H_{17})

Figure 3. Surface tension (γ) as a function of the logarithm of the molar concentration of the bis-charged salts.

imum in the case of the charged benzimidazolium substituent.

Compounds **5-19**, due to the presence of a long alkyl chain and of a positive charge, show a reasonable surface activity. In Tables I and III the surface properties of their water solutions are reported. It is worth emphasizing that the mono salts **5-7** do not reach a CMC (critical micellar concentration) and hence do not form micellar aggregates. In Figure **2** a plot of log c versus γ is reported. The surface tension decreases linearly with log c, indicating that, within the concentration range amenable to examination, no micellar aggregates are being formed. Using Gibbs' equation (**1**), the surface excess concentration Γ (in

$$\Gamma = \frac{1}{2.303\, m\, RT}\left(-\frac{\delta\gamma}{\delta \log c}\right)_T \qquad (1)$$

mol·cm^{-2}) at the air-water intervace is calculated (m = 2).

$$A_{min} = \frac{10^{16}}{N_A\ \Gamma} \qquad (2)$$

From equation (**2**) (7) the minimum areas per molecule (A_{min} in Å^2) can be determined (N_A = Avogadro's number). The γ/log c correlation for compounds **8-10** (figure 3) displays a different feature.

Due to the presence of two positive charges, micellar systems arise as evidenced by the discontinuity in the curves corresponding to the CMC. The minimum areas per molecule resulting from equations (**1**) and (**2**) (M = 3) are larger than those of monomethiodides. The CMC values are functions of the aliphatic chain length.

The dyes also behave like the bis-methiodides from which they are derived. The areas per molecules of unsymmetrical dyes are larger than those of salts and styryl dyes, and the CMC values are slightly lower than those of bis quaternary salts.

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EXPERIMENTAL

The nmr spectra were obtained with a Varian T 60 spectrometer in DMSO-d_6 solution (6%) using TMS as an internal standard. Electronic spectra were recorded in ethanol on a Pye Unicam SP 8-100 spectrophotometer. Surface tension measurements were performed with Dognon-Abribat tensiometer. The tlc were performed on silica gel 60 F 254 (Merck) plates using BAW (4:5:1) as eluent.

Compound **1** was prepared as indicated in reference (1).

Compounds **2-4** were prepared by reacting **1** (0.05 mole) with the suitable alkyl bromide (0.05 mole) in dimethylformamide (50 ml) stirring and refluxing for ten hours. The reaction mxiture was cooled, poured into water, repeatedly extracted with ligroin (2 liters); the organic layer was dried over sodium sulphate and reduced to a small volume. The residue

was twice crystallized from ethanol (compounds **2** and **3**) and vacuum distilled (compound **4**).

Compounds **5-7** were prepared by refluxing the corresponding free base **2-4** with a large excess of methyl iodide over a period of twelve hours. The reaction mixture, after cooling, was treated with a large excess of diethyl ether. The crude precipitate was collected, washed with diethylether, and crystallized from ethanol.

The quarternization to compounds **8-10** was performed refluxing over a period of four hours the appropriate bases **2-4** in toluene with an excess of dimethylsulphate. The solvent was removed, the residue slurried with diethyl ether, filtered and mixed with a saturated solution of potassium iodide. The solid was collected and crystallized from ethanol.

Styryl dyes were prepared by refluxing for 40 minutes in absolute ethanol (piperidine acetate as catalyst) the methiodides **8-10** with *p*-dimethylaminobenzaldehyde (molar ratio 1:1). After cooling, diethyl ether was added and the product was collected, washed with diethyl ether and crystallized from ethanol.

Unsymmetrical dyes were prepared by refluxing the methiodides for 45 minutes in absolute ethanol (triethylamine as catalyst) with (3-methyl-2-benzothiazolynilydene)ethanal (benzothiazole unsymmetrical dyes) or 1-methyl-4-acetanilidovinylquinolinium iodide (lepidine unsymmetrical dyes). The reaction mixture was kept overnight, the solid collected and crystallized from ethanol (dyes **14-16**) or from acetic anhydride (dyes **17-19**).

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